

2. (Amended) The method according to Claim 1, wherein the inhibitor of elastase-like enzymes is [another inhibitor of elastase-like enzymes than] not a matrix metalloproteinase inhibitor.

3. The method according to Claim 1, wherein the inhibitor of elastase-like enzymes is an inhibitor of an elastase-like enzyme derived from a dermoepidermal fibroblast.

4. The method according to Claim 1, wherein the neutral endopeptidase inhibitor is an inhibitor of a neutral endopeptidase derived from a dermoepidermal fibroblast.--

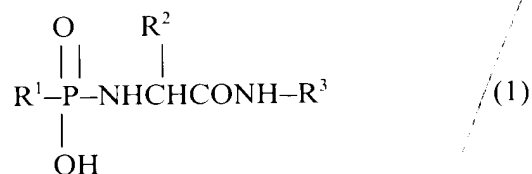
Please add the following new claims:

5. The method according to Claim 1, wherein said subject is a human.

6. The method according to Claim 1, wherein said inhibitor of elastase-like enzymes

or a neutral endopeptidase inhibitor is selected from the group consisting of:

phosphoric acid derivatives having the following formula (1):



wherein R<sup>1</sup> is a hydrogen atom, a hydroxyl group, a hydrocarbon group which may be substituted, or a sugar residue which may be substituted,

R<sup>2</sup> is a hydrogen atom, a hydrocarbon group which may be substituted, or a sugar residue which may be substituted, and

R<sup>3</sup> is a hydrogen atom or a -CH(R<sup>4</sup>)COOH in which R<sup>4</sup> is a hydrogen atom or a hydrocarbon group which may be substituted, and salts thereof; and mercaptopropionamide derivatives having the following formula (2):



wherein R<sup>5</sup> is a hydrogen atom or an acyl group, R<sup>6</sup> is a hydrogen atom or a hydrocarbon group which may be substituted, and

R<sup>7</sup> is a hydrogen atom, a carboxyl group, an alkoxycarbonyl group, a hydrocarbon group which may be substituted, a heterocyclic group which may be substituted, or an acyl group, and n is a number of 1 to 20.

8. The method according to Claim 7, wherein in said formulas (1) and (2), the hydrocarbon groups which are represented by R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>6</sup> and R<sup>7</sup> are each independently saturated or unsaturated hydrocarbon groups having 1-24 carbons selected from the group consisting of alkyl, alkenyl, alkynyl, cyclic alkyl, cyclic alkenyl, aromatic hydrocarbon and aralkyl groups.

9. The method according to Claim 7, wherein in said formulas (1) and (2), the hydrocarbon groups which are represented by R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>6</sup> and R<sup>7</sup> are each independently selected from the group consisting of linear or branched alkyl groups having 1 to 12 carbon atoms, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, isoamyl, 5- to 7-membered alicyclic alkyl groups, cyclopentyl, cyclohexyl, aromatic hydrocarbon groups having 6 to 14 carbon atoms, phenyl, naphthyl groups, alkyl groups having 1 to 5 carbon atoms which have been substituted by an aromatic hydrocarbon group having 6 to 12 carbon atoms, 2-phenylethyl (=phenethyl), 2-(1-naphthyl)ethyl, and 2-(2-naphthyl)ethyl.

10. The method according to Claim 7, wherein in said formulas (1) and (2), at least one of the hydrocarbon groups which are represented by R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup>, R<sup>6</sup> and R<sup>7</sup> is substituted with one or more substituents selected from the group consisting of halogen atom, a hydroxyl

group, alkoxyl group, acyl group, an amino group which may be protected, heterocyclic groups, chlorine, bromine, iodine, alkoxyl groups having 1 to 12 carbon atoms, methoxy, ethoxy, isopropoxy, alkanoyl groups having 1 to 12 carbon atoms, acetyl, propionyl, butyryl, C<sub>1-8</sub>-acylamino, C<sub>1-6</sub>-alkylamino di-(C<sub>1-6</sub>-alkyl)amino; 5- to 14-membered monocyclic or fused ring groups having, as heteroatom(s), 1 to 3 nitrogen, oxygen and/or sulfur atoms; pyridyl, pyridazinyl, furyl, thienyl, indolyl, thiazolyl, imidazolyl, benzofuryl, and benzothienyl groups.

11. The method according to Claim 7, wherein in said formula (1), said sugar residues are selected from the group consisting of monosaccharide residues and oligosaccharide residues.

10. The method according to Claim 7, wherein said sugar residues are substituted with one or more substituents selected from the group consisting of alkyl, acyl and aralkyl groups.

12. The method according to Claim 7, wherein said sugar residues are substituted with one or more substituents selected from the group consisting of linear or branched alkyl groups having 1 to 12 carbon atoms, n-propyl, isopropyl, n-butyl, isobutyl, tert-butyl, isoamyl, 5- to 7-membered alicyclic alkyl groups, cyclopentyl, cyclohexyl, alkanoyl groups having 1 to 12 carbon atoms, acetyl, propionyl, butyryl, alkyl groups having 1 to 5 carbon atoms which have been substituted by an aromatic hydrocarbon group having 6 to 12 carbon atoms, 2-phenylethyl (= phenethyl), 2-(1-naphthyl)ethyl, and 2-(2-naphthyl)ethyl groups.

13. The method according to Claim 7, wherein in said formula (2), the acyl groups represented by R<sup>5</sup> and R<sup>7</sup> are each independently selected from the group consisting of alkanoyl groups and arylcarbonyl groups.

15. The method according to Claim 7, wherein in said formula (2), the acyl groups represented by  $R^5$  and  $R^7$  are each independently selected from the group consisting of alkanoyl groups having 1 to 12 carbon atoms, acetyl, propionyl, butyryl, arylcarbonyl groups having 7 to 15 carbon atoms, benzoyl, substituted benzoyl, naphthylcarbonyl, and substituted naphthylcarbonyl groups.

16. The method according to Claim 15, wherein said substituted benzoyl and naphthylcarbonyl groups are substituted with a substituent selected from the group consisting of  $C_{1-6}$  alkyl,  $C_{1-6}$  alkoxy, halogen atom, an amino group, a hydroxyl group and  $C_{1-6}$  alkanoyloxy group.

17. The method according to Claim 7, wherein in said formula (2), said n is 1 to 6.

18. The method according to Claim 7, wherein in said formula (2), the heterocyclic group represented by  $R^7$  is selected from the group consisting of a 5- to 14-membered monocyclic or fused ring group having, as heteroatom(s), 1 to 3 atoms selected from the group consisting of nitrogen, oxygen and sulfur; pyridyl, pyridazinyl, furyl, thienyl, indolyl, thiazolyl, imidazolyl, benzofuryl, benzothienyl, pyrrolidinyl, piperidinyl, morpholinyl and piperazinyl groups.

19. The method according to Claim 7, wherein in said formula (2), the heterocyclic group represented by  $R^7$  is substituted with a substituent selected from the group consisting of a halogen atom, a hydroxyl group, alkoxy group, acyl group and an amino group which may be protected heterocyclic groups, chlorine, bromine, iodine, alkoxy groups having 1 to 12 carbon atoms, methoxy, ethoxy, isopropoxy, alkanoyl groups having 1 to 12 carbon atoms, acetyl, propionyl, butyryl,  $C_{1-8}$ -acylamino,  $C_{1-6}$ -alkylamino di- $(C_{1-6}$ -alkyl)amino; 5- to 14-membered monocyclic or fused ring groups having, as heteroatom(s), 1 to 3 nitrogen,

oxygen and/or sulfur atoms; pyridyl, pyridazinyl, furyl, thienyl, indolyl, thiazolyl, imidazolyl, benzofuryl, and benzothienyl groups.

20. The method according to Claim 7, wherein in said formula (2), the alkoxycarbonyl group represented by  $R^7$  is selected from the group consisting of alkoxycarbonyl groups wherein the alkoxy moiety of which has 1 to 12 carbon atoms, methoxycarbonyl, ethoxycarbonyl, isopropoxycarbonyl and butoxycarbonyl groups.

21. The method according to Claim 7, wherein said salts of formulas (1) and (2) are selected from the group consisting of alkali metal salts, alkaline earth metal salts, organic amine salts, amino acid salts, sodium salt, potassium salt, calcium salt, magnesium salt, ammonium salts, methylamine salt, triethylamine salt, pyridinium salt, arginine salt, lysine salt and histidine salt.--

#### **BASIS FOR THE AMENDMENTS**

Claim 1 has been amended to clarify the nature in which the hair growth inhibitor is administered. The amendment is supported by Claim 5 as originally filed. Claim 5 has been canceled accordingly.

Claim 2 has been amended for clarity and as suggested by the Examiner. Support is found in the claim as originally filed.

New Claims 6-21 have been added to narrower and more preferred embodiments of the invention.

Claim 6 is supported at page 3 of the specification, lines 20-23.

Claim 7 is supported at page 5 of the specification, lines 2-18 and page 7, line 17 to page 8, line 1.

Claim 8 is supported at page 5 of the specification, lines 19-26 and page 8, lines 15-17.

Claim 9 is supported at the paragraph bridging pages 5-6 of the specification and page 8, lines 15-17.

Claim 10 is supported at the paragraph bridging pages 6-7 of the specification and page 8, lines 15-17.

Claims 11-13 are supported at page 7 of the specification, lines 8-12 and the paragraph bridging pages 5-6.

Claims 14-17 are supported at page 8 of the specification, lines 2-14.

Claim 18 is supported at the paragraph bridging pages 8-9 of the specification.

Claim 19 is supported at page 8, line 25 to page 9, line 4 of the specification and at the paragraph bridging pages 6-7.

Claim 20 is supported at page 9 of the specification, lines 5-9.

Claim 21 is supported at the paragraph bridging pages 9-10 of the specification.

No new matter is believed to be introduced to the application by entry of the amendments. Upon entry of the amendments, Claims 1-4 and 6-21 will be active. Entry and favorable consideration are respectfully requested.

#### **REQUEST FOR RECONSIDERATION**

Applicants wish to thank Examiner Weber for the courteous and helpful discussion held with Applicants' Japanese and U.S. representatives on May 30, 2000. Applicants also wish to thank Examiner Weber for indicating that the claim amendments submitted herewith would be sufficient to remedy the rejection under 35 U.S.C. §112, second paragraph. It was

Applicants' U.S. representative's impression that the claims as amended herein would be favorably considered over the Mato et al reference, but that the recently-filed Information Disclosure Statement had not yet been considered. The discussion is summarized below.

The rejection of Claims 1-5 under 35 U.S.C. §103(a) over Mato et al is respectfully traversed. As was discussed during the interview, the reference relates only to the promotion of hair growth. Accordingly, the reference is deficient in that it does not provide any motivation to inhibit hair growth or any reasonable expectation that hair growth might be successfully inhibited by, for example, the topical application of an inhibitor of elastase-like enzymes. The reference is also completely silent regarding a neutral endopeptidase inhibitor, in further contrast to the claims. As was noted during the interview, the reference at best invites experimentation, but it is respectfully submitted that an obviousness rejection is unsustainable over the teachings of this reference.

Of the several references referred to in the Official Action to establish the state of the art, Applicants note none of the references refer to the inhibition of hair growth by the topical application of an inhibitor of elastase-like enzymes. As was pointed out during the interview, the closest reference appears to be U.S. 5,962,466, which relates to the reduction of hair growth using inhibitors of matrix metalloproteinase. However, this reference has not been cited against the claims.

As was pointed out at the interview, Applicants respectfully submit that even a *prima facie* obviousness rejection would be overcome by the data already of record in the specification.

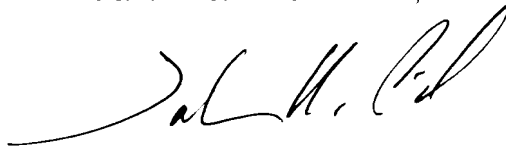
Accordingly, for the reasons given above, it is believed that the rejection over Mato et al should be withdrawn.

The rejection of Claims 1-5 under 35 U.S.C. §112, second paragraph, is obviated by amendment. Claims 1 and 2 have been amended such that they are now believed to particularly point out and distinctly claim that which is regarded as the invention, and Claim 5 has been canceled. Withdrawal of the rejection is therefore respectfully requested.

Applicants respectfully submit that the above-identified application is now believed to be in condition for allowance, and early notice of such action is earnestly solicited. Should the Examiner wish to indicate any allowable subject matter, or otherwise wish to discuss this case, he is respectfully invited to contact Applicants' below-signed U.S. representative by telephone, who would be happy to assist in expediting any further prosecution deemed necessary.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.

A handwritten signature in dark ink, appearing to read 'N. F. Oblon', written in a cursive style.

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